

Application No.: PCT/IN03/000290

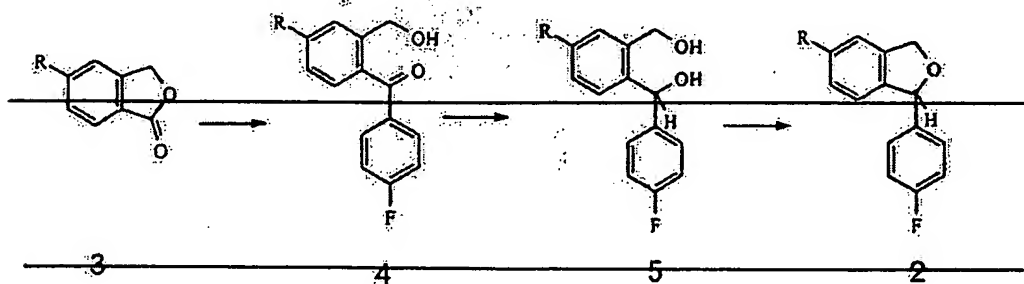
AMENDMENT TO THE CLAIMS:

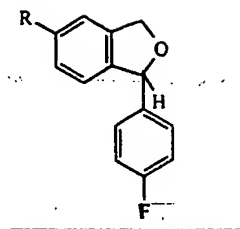
This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Currently amended) A process for the preparation of a 5-substituted-1-(4-fluorophenyl)-1,3- dihydroisobenzofuran of Formula 2, an intermediate for the manufacture of citalopram, which process comprises comprising:

- (a) carrying out a Grignard reaction on a ~~corresponding~~ 5-substituted phthalide of Formula 3 in a co-solvent system, comprising adding (i) prepared 4-fluorophenyl magnesium halide in an ether solvent to (ii) ~~the~~ a 5-substituted phthalide in a suitable an organic co-solvent to the ether solvent, to form a ~~corresponding~~ 4-substituted- 2-hydroxymethyl-4'-fluorobenzophenone of Formula 4,
- (b) carrying out a ketone reduction of the 4-substituted-2-hydroxymethyl-4'-fluorobenzophenone of Formula 4 following the Grignard reaction, to form a ~~corresponding~~ 4-substituted-2-hydroxymethylphenyl-1-(4-fluorophenyl) methanol of Formula 5, and
- (c) carrying out a cyclisation reaction on the 4-substituted-2-hydroxymethylphenyl-1-(4-fluorophenyl) methanol of Formula 5 following the reduction reaction, to form ~~said intermediate of Formula 2~~ a compound having the structure:





wherein R represents Br or CN.

2. (Currently amended) A process according to claim 1, wherein the co-solvent is selected from the group consisting of an aliphatic chlorinated solvent, or an aromatic chlorinated solvent or and an aromatic hydrocarbon.
3. (Currently amended) A process according to claim 2, wherein the co-solvent is an aliphatic or aromatic chlorinated solvent selected from the group consisting of methylene dichloride, ethylene dichloride, trichloroethane, carbon tetrachloride, chloroform, chlorobenzene, dichlorobenzene, and mixtures thereof.
4. (Currently amended) A process according to claim 3, wherein the co-solvent is at least one of methylene dichloride or and chloroform.
5. (Currently amended) A process according to claim 2, wherein the co-solvent is an aromatic hydrocarbon selected from the group consisting of toluene, benzene, xylene, and mixtures thereof.
6. (Currently amended) A process according to Claim 1 ~~any of the preceding claims,~~ wherein the ether solvent and co-solvent are both dry.
7. (Currently amended) A process according to Claim 1 ~~any of the preceding claims,~~ wherein the volumetric ratio of ether solvent to co-solvent is between 3:10 and 6:7.
8. (Currently amended) A process according to Claim 1 ~~any of the preceding claims,~~ wherein the ether solvent is selected from the group consisting of 1,4-dioxane, diethylether, dimethoxyethane or and tetrahydrofuran (THF).
9. (Currently amended) A process according to Claim 1 ~~any of the preceding claims,~~ wherein in the ketone reduction step (b), between 0.25 and to 1.0 molar equivalents of sodium borohydride are used as reducing agent.

10. (Currently amended) A process according to claim 9, wherein in the ketone reduction step (b), 0.5 molar equivalents of sodium borohydride are used as reducing agent.

11. (Currently amended) A process according to Claim 1 ~~any of the preceding claims~~, wherein the cyclisation reaction (c) comprises the use of concentrated hydrochloric acid or an organic acid selected from the group consisting of methanesulfonic acid, benzenesulfonic acid and para-toluene sulfonic acid (PTSA).

12. (Original) A process according to claim 11, wherein the acid is used in a catalytic amount.

13. (Original) A process according to claim 12, wherein the acid is PTSA in a catalytic amount of 5 to 10% w/w with respect to the 5-substituted phthalide.

14. (Currently amended) A process according to Claim 1 ~~any of the preceding claims~~, wherein the Grignard reaction (a) is carried out at a temperature of from -6°C to -2°C.

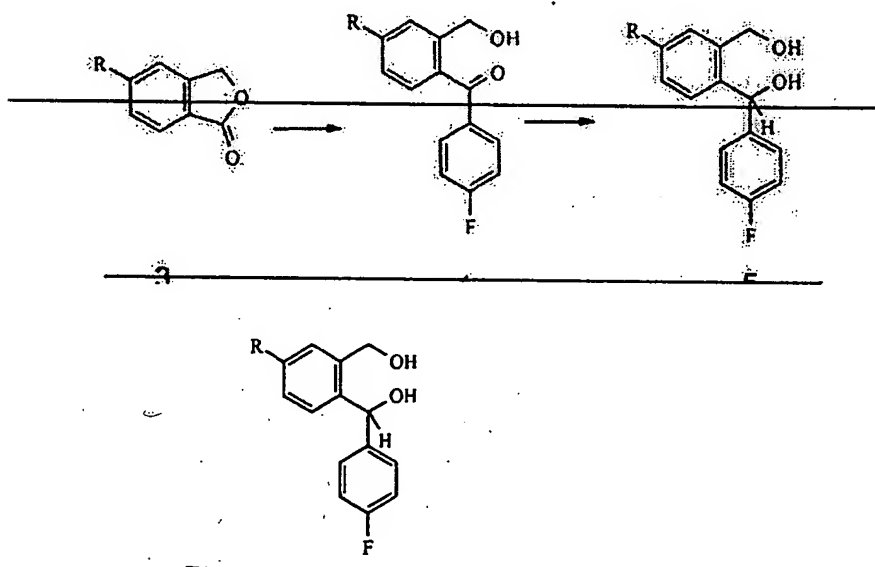
15. (Currently amended) A process according to Claim 1 ~~any of the preceding claims~~, wherein in the Grignard reaction (a), the molar ratio of 4-fluorophenyl magnesium halide to 5-substituted phthalide is 1:1 to 1.4:1.

16. (Currently amended) A process according to Claim 1 ~~any of the preceding claims~~, wherein the entire process, comprising Grignard reaction (a), reduction reaction (b) and cyclisation reaction (c), is carried out in a reaction vessel without isolation of intermediates from solution.

17. (Currently amended) A process for preparation of 4-bromo-2-hydroxymethylphenyl-1-(4-fluorophenyl) methanol or 4-cyano-2-hydroxymethylphenyl-1-(4-fluorophenyl) methanol ~~of Formula 5, which process comprises~~ comprising:

- (a) carrying out a Grignard reaction on a ~~corresponding~~ 5-substituted phthalide ~~of Formula 3~~ in a co-solvent system, comprising adding (i) ~~prepared~~ 4-fluorophenyl magnesium halide in an ether solvent to (ii) ~~the~~ a 5-substituted phthalide in a suitable organic co-solvent to the ether solvent, to form a ~~corresponding~~ 4-substituted-2-hydroxymethyl-4'-fluorobenzophenone ~~of Formula 4~~, and

- (b) carrying out a ketone reduction of the 4-substituted-2-hydroxymethyl-4'-fluorobenzophenone of Formula 4 with sodium borohydride, to form 4-bromo-2-hydroxymethylphenyl-1-(4-fluorophenyl) methanol or 4-cyano-2-hydroxymethylphenyl-1-(4-fluorophenyl) methanol of Formula 5 a compound having the structure:



wherein R represents Br or CN.